IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
Li *et al.*	Art Unit: 1646
Appl. No.: 08/852,824	Examiner: Basi, N.
Filed: May 7, 1997	Atty. Docket: 1488.1220000/EKS/EJH
For: **Human G-Protein Coupled Receptors**	

Declaration of Steven M. Ruben Under 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

1. I, Steven M. Ruben, hereby declare and state as follows:

2. I am a named inventor of the captioned application, which is assigned to Human Genome Sciences, Inc. (HGS), and I am presently employed by HGS. The work described below was done by myself, under my supervision, or as part of a collaborative research effort with other individuals at HGS.

Human Epstein Barr Virus-Induced G-Protein Coupled Receptor-2 (EBI-2)

3. We obtained a cDNA clone encoding a human Epstein Barr virus-induced G-protein coupled receptor-2 (EBI-2) by screening a human hippocampus cDNA library. This clone was designated HHPGS02. We determined nucleotide sequence information for the HHPGS02 clone, as described below, using sequencing methods which were routine and publicly available as of the May 7, 1997 filing date of the present application. The HHPGS02 clone that we obtained this sequence information from was deposited with the American Type Culture

Collection (ATCC) on April 28, 1997 and was given ATCC Accession No. 209003. (*See* Attachment A.)

4. Evidence that the human HHPGS02 cDNA was deposited at the ATCC as Accession No. 209003 is provided by comparing the ATCC Deposit Receipt (Attachment A) with the information provided in the IRIS notebook page (entitled "Sequence Worksheet") included herewith as the first page of Attachment B.[1] The section of the page entitled "Sequence Information" corresponds clone HHPGS02[2] with the "HGS Code," 405439. HGS Code 405439 represents a particular sequence entry in IRIS for cDNA clone HHPGS02. HGS Code 405439 appears as the identifier on the ATCC deposit receipt. (*See* Attachment A.) This indicates that the clone used to obtain the sequence information of HGS Code 405439 was deposited. In other words, even though, as explained below, SEQ ID NO:1 and SEQ ID NO:2 in the Sequence Listing of the present application as originally filed, had typographical errors due to attorney error, the human HHPGS02 cDNA clone used to obtain the original, correct sequence data was deposited at the ATCC.

5. Attachment B provides four pages of data from the IRIS electronic notebook which shows the sequencing results of the human EBI-2 cDNA clone *(i.e.*, HHPGS02). The HHPGS02 sequence was obtained using a 373 Automated DNA sequencer (Applied Biosystems, Inc.). Sequencing accuracy using this method is predicted to be greater than 97%.

6. The information obtained from the HHPGS02 sequencing run differs from the Sequence Listing currently on file in the present application at four positions. In particular, SEQ

---

[1]IRIS is an electronic notebook used by HGS scientists to enter and maintain sequence data.

[2]The "XX" designation added to the 7-character clone ID on the IRIS Notebook pages, e.g., HHPGS02, merely indicates that the sequence of that clone is full-length.

ID NO:1 contains typographical errors at the following nucleotide positions: position 242, which should be A rather than T; position 266, which should be C rather than A; position 1870 (in the 3' untranslated region), where a T should be deleted, and position 2206, where an N should be deleted. These typographical errors in the nucleotide sequence result in the following errors to the encoded amino acid sequence depicted as SEQ IDNO:2: an isoleucine at position 6 should be replaced with an asparagine, and an asparagine at position 14 should be replaced with a threonine. Both of these changes are reflected in the HHPGS02 amino acid sequence data shown on the third and fourth pages of Attachment B, as well as in an amino acid alignment originally filed with the present application as Figure 2.

7. I believe that the actual nucleotide sequence of the human HHPGS02 cDNA clone is the same as that originally entered in the IRIS notebook.

8. I am of the opinion that the correct EBI-2 nucleotide and amino acid sequences would have been apparent to one skilled in the art in possession of ATCC Deposit No. 209003 and the data from the HHPGS02 sequencing run, as of the May 7, 1997 filing date of the present application. This is so because the correct EBI-2 coding sequence can be readily determined from the deposited clone and methods for sequencing this clone were routine in the art in May of 1997.

Human Endothelium Differentiaion Gene-1-Like (EDG-1-Like) G-Protein Coupled Receptor

9. We obtained a cDNA clone encoding a human endothelium differentiation gene-1-like (EDG-1-like) G-protein coupled receptor by screening a cDNA library derived from human activated neutrophils. This clone was designated HNFDL69. We determined nucleotide sequence information for the HNFDL69 clone, as described below, using sequencing methods which were routine and publicly available as of the May 7, 1997 filing date of the present application. The

HNFDL69 clone that we obtained this sequence information from was deposited with the American Type Culture Collection (ATCC) on April 28, 1997 and was given ATCC Accession No. 209004 (*See* Attachment A.)

10. Evidence that the human HNFDL69 cDNA was deposited at the ATCC as Accession No. 209004 is provided by comparing the ATCC Deposit Receipt (Attachment A) with the information provided in the IRIS notebook page (entitled "Sequence Worksheet") included herewith as the first page of Attachment C. The section of the page entitled "Sequence Information" corresponds clone HNFDL69 with the "HGS Code" 563238. HGS Code 563238, represents a particular sequence entry in IRIS for cDNA clone, HNFDL69. HGS code 563238 appears as the identifier on the ATCC deposit receipt. (*See* Attachment A.) This indicates that the clone used to obtain the sequence information of HGS Code 563238 was deposited. In other words, even though, as explained below, SEQ ID NO:3 and SEQ ID NO:4 of the Sequence Listing in the present application as originally filed, had typographical errors due to attorney error, the human HNFDL69 cDNA clone used to obtain the original, correct sequence data was deposited at the ATCC.

11. Attachment C provides three pages of data from the IRIS electronic notebook which shows the sequencing results of the human EDG-1-like cDNA clone *(i.e.*, HNFDL69). The HNFDL69 sequence was obtained using a 373 Automated DNA sequencer (Applied Biosystems, Inc.). Sequencing accuracy using this method is predicted to be greater than 97%.

12. The information obtained from the HNFDL69 nucleotide sequencing run differs from the Sequence Listing currently on file in the present application in two positions. In particular, SEQ ID NO:3 contains typographical errors at the following nucleotide positions: position 828, which should be T rather than C; and position 831, which should be T rather than

A. Note that this latter typographical error introduced a stop codon into the open reading frame, causing the amino acid sequence, as translated from the sequence with the typographical error, to stop at position 260. Accordingly, these typographical errors in the nucleotide sequence result in the following errors to the encoded amino acid sequence depicted as SEQ IDNO:4: the serine at position 260 should be replaced with phenylalanine, and the translation should continue to amino acid 384, as depicted in the original translation provided on the third page of Attachment C. SEQ ID NO:4 further contains typographical errors at the following amino acid positions: position 191, which should be Asp rather than Asn, position 202, which should be Lys rather than Arg, and position 204, which should be Tyr rather than Thr. In addition, the translation should start with the Met at position 1, rather than the Ala at position -16. Both of the nucleotide sequence changes are reflected in the HNFDL69 nucleotide sequence data shown on the first and second pages of Attachment C, and the amino acid sequence changes are reflected in the HNFDL69 amino acid sequence data shown on the third page of Attachment C. In addition, The amino acid sequence data is reflected in an amino acid alignment originally filed with the present application as Figure 4, except for five residues at the 3' end of the polypeptide. These latter five residues are not in the alignment simply because they did not align with the second sequence in Figure 4, i.e., SEQ ID NO:18.

13. I believe that the actual nucleotide sequence of the human HNFDL69 cDNA clone is the same as that originally entered in the IRIS notebook.

14. I am of the opinion that the correct EDG-1-like nucleotide and amino acid sequences would have been apparent to one skilled in the art in possession of ATCC Deposit No. 209004 and the data from the HNFDL69 sequencing run, as of the May 7, 1997 filing date of the present application. This is so because the correct EDG-1-like coding sequence can be readily

determined from the deposited clone and methods for sequencing this clone were routine in the art in May of 1997.

15. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the Unites States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereupon.

7/15/99
Date

Steven M. Ruben